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TECHNICAL EVALUATION OF RNA-SEQ AND MICROARRAY APPROACHES IN COMPARATIVE TRANSCRIPTOMICS ANALYSIS OF CHO CELLS

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RNA-Seq has been replacing microarrays as the primary tool for comparative transcriptomics analysis. However, successful application of RNA-Seq to profile Chinese hamster ovary cells (CHO), the leading industrial cell line for recombinant protein production, was limited, primarily because of the inadequacy of genomic information for CHO cells. A compromised alternative to perform gene expression analysis and pathway or GO enrichment analysis in CHO cells was to map CHO genes to their mouse orthologs. Recent increased availability of CHO genomic references and the KEGG pathway reference for Chinese hamster has enabled direct gene expression analysis in the genome context of CHO cells. This has also enabled evaluation of the comparability of transcriptomics analysis by using different genome references, methods, and platforms. In this study, we applied both microarray and RNA-Seq technologies to profile two CHO cell lines with similar proliferation index but diverse recombinant protein productivity. Molecular signatures such as differentially expressed genes and KEGG pathways were identified to help understand performance differences despite similar cultivation conditions. Our analysis shows that using mouse orthologs for gene expression analysis generates comparable results as using the Chinese hamster genome reference, which provides justification for most previous transcriptomic studies. Additionally, when compared to microarray analysis, RNA-Seq provides superior outcomes due to its wider dynamic gene expression range and higher genome coverage. We also evaluated sample number and sequencing depth, two important parameters in RNA-Seq based comparative transcriptomics, and our results indicated that increasing replicates was more efficient than increasing sequencing depth for increased power and accuracy in differential gene expression analysis. Overall, this study provides multiple practical insights for improved execution of comparative transcriptomics analysis to understand CHO cells at gene expression level.